Falling: should one blame the heart?

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CHAPTER FIVE

AF IS ASSOCIATED WITH SELF-REPORTED SYNCOPE AND FALLS IN A GENERAL POPULATION COHORT
AF IS ASSOCIATED WITH SELF-REPORTED SYNCOPE AND FALLS IN A GENERAL POPULATION COHORT

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ABSTRACT

BACKGROUND

Syncope is an important, but underestimated clinical problem in older persons. It is often overlooked in clinical practice or mistaken for falls. Atrial fibrillation (AF) is the most common cardiac arrhythmia, but little evidence exists regarding the association between AF, falls and syncope in the general population.

METHODS

Cross-sectional analyses within a population sample of people aged 50+, taken from The Irish Longitudinal Study on Ageing. Ten-minute electrocardiogram recordings (n=4885) were analysed to detect AF. Syncope (self-reported faints or blackouts) and falls in the past year, comorbidities, health measures and medications were gathered through computer-aided personal interviews. Multivariable logistic regression was performed to study associations between AF, falls and syncope.

RESULTS

Mean age was 62 years (range 50-91), 54% were female. Prevalence of AF was 3%, increasing to 8% in participants aged 75+. Of participants, 5% (n=223) reported syncope and 20% (n=972) reported falls. After adjustment for confounders, AF was significantly associated with faints and blackouts (OR 2.0 [95%CI 1.0–3.9]). After stratification by age category, we found that this association was strongest and only significant in participants aged 50-64 years (OR 4.4 [1.5–12.6]). Stratified for age group, AF was significantly associated with falls in participants aged 65-74 years (OR 2.0 [1.0–4.1]).

CONCLUSIONS

Adults aged 50+ with self-reported syncope, and adults aged 65-74 years with falls are twice as likely to have AF at physical examination. These associations are independent of stroke, cardiovascular and psychotropic drugs and other confounders. Further longitudinal studies are needed to explore this association and potential causality further.
INTRODUCTION

Falls in older people and their related injuries form a significant health care burden 1,2. Several risk factors for falls in older persons have been recognized, but controversy still remains regarding the importance of heart rhythm abnormalities as a modifiable risk factor for falls 3. Given that there is emerging evidence of overlap between the symptoms of falls and syncope 3, fall-prevention guidelines recommend cardiovascular evaluation as part of comprehensive falls assessment 3. Despite this recommendation, cardiovascular risk factors for falls remain under evaluated in clinical practice 4.

Arrhythmias are an important cardiac cause of syncope as they impair hemodynamic function, resulting in a critical decrease in cardiac output and cerebral blood flow 5. Atrial fibrillation (AF) is the most common cardiac arrhythmia in adults with its prevalence rising from 1-2% in the general population to nearly 5% in community-dwellings aged 65+ 6,7. To date, AF has only been linked to recurrent syncope in a general population study 8. An association between AF and non-accidental falls was reported in a sample of patients attending the emergency department (ED) following a fall 9. As yet, no studies have investigated the association between AF and falls on a general population level.

If AF is indeed associated with falls and syncope, this would provide new evidence for a potentially treatable risk factor for falls and syncope. In this study we investigated whether AF was more common in community-dwelling older adults with a history of a fall, faint or blackout in the past year.

METHODS

Study design
The Irish Longitudinal Study on Ageing (TILDA) is a nationally representative prospective cohort study comprising community-dwellings aged 50+, resident in the Republic of Ireland. The current cross-sectional study was based on the first wave of data, collected between 2009 and 2011. Further details of the study are published elsewhere 10. Data were collected by a personal interview, a self-completion questionnaire and a physical health assessment conducted in a health centre. Ethical approval was obtained with the Trinity College Dublin Research Ethics Committee; all participants provided signed informed consent prior to participating.

Falls and syncope
Participants were asked how often they had a fall, faint or blackout in the past year. Falls were defined as one or more falls in the past year. Syncope was defined as one or more faints or blackouts.

Covariate information
The following covariates were taken from the home interview or self-completion questionnaire: age, gender, highest level of education, smoking, alcohol consumption and body mass index (BMI, kg/m2). Depressive symptoms were defined as a score of ≥16 on the Centre for Epidemiological Studies Depression-scale 11. Disability was defined as any disability from the lists of (Instrumental) Activities of Daily Living (iADL/ADL) 12. For cognitive function, the Mini-Mental State Examination (MMSE) was used. Other comorbidities included lung disease, angina, myocardial infarction, heart failure, diabetes mellitus, stroke, transient ischemic attack and cardiac arrhythmias.

The following covariates were gathered during the health assessment. Corrected visual acuity (VA) was measured in both eyes using a logMAR chart 13. Blood pressure was measured from two recordings, using a sphygmomanometer on the upper arm in the seated position. Gait speed was measured using a computerised walkway (GAITRite©, CIR Systems Inc, New York, USA). Medication use was recorded during the home interview and confirmed by cross-checking of medication labels; Anatomical Therapeutic Classification (ATC) codes were recorded 14. Medication categories included were psychotropic drugs (‘N05*’, ‘N06*’) and cardiovascular medications: Cardiac therapy (‘C01*’), antihypertensives (‘C02*’).
Evaluation of AF
Ten-minute surface electrocardiograms (ECG) were conducted during the health assessment (Medilog Darwin®, Schiller, Baar, Switzerland). Two clinicians screened ECGs for AF independently, according to ESC guidelines. In case of inter-rater disagreement, a cardiologist made final judgement.

Statistical analysis
Prevalence calculations were weighted with respect to age, sex and education to the Quarterly National Household Survey (2010) to ensure that data were nationally representative, and further weighted by health status and socio-demographic factors to account for those who did not attend a health assessment. Baseline differences between groups were tested using an independent t-test for continuous variables and chi-square tests for dichotomous variables. Mann-Whitney-U test was used for continuous variables with non-normal distribution.

Multivariable logistic regression models were used to assess the association between AF and falls, and AF and syncope. The bivariate model included AF only. Model 1 included age, gender and education. In model 2, other potential confounders were added. Variables that changed the point estimate of the age, gender and education-adjusted model with AF and falls or syncope by more than 5% were added to the multivariable model, together with important risk factors for falls and syncope. Covariates that were tested for potential confounding were: age, ADL disability, BMI, gait speed, depressive symptoms, visual acuity, MMSE score, stroke, use of psychotropic drugs and use of cardiovascular drugs. To account for the potential role of AF-related cardiovascular conditions as confounders, an additional model was tested that included hypertension, congestive heart failure, heart attack and heart murmur.

Ordered logistic regression was used to investigate a dose response in the associations between AF and number of falls and syncope (categorized as none, one or ≥2 events). Odds ratios were interpreted as the odds of observing a response in higher falls or syncope risk categories, compared to lower risk categories. Test of parallel lines was used to assess the assumption of proportional odds. The same covariates as for logistic regression analyses were used in the multivariable models. A p-value of <0.05 was used as the threshold for statistical significance. Statistical analyses were performed using IBM SPSS Statistics (Version 18.0, IBM Corp. Released 2010. Armonk, NY).

RESULTS
In total, 8175 participants aged 50+ were recruited to the study. Of these, 5036 underwent a health assessment; 4890 (97%) underwent ECG recording. Information on falls was available in 4888 participants, and on syncope (self-reported faints or blackouts) in 4886 participants. Mean age was 61.9 years (SD 8.4) and 54% (n=2647) were female. Of participants, 20.3% (n=972) reported one or more falls and 4.9% (n=223) reported one or more faints or blackouts.

Prevalence of AF was 3.0% (n=118), increasing from 1.0% in participants aged 50-64 years, to 4.1% in those aged 65-74 years, to 7.8% in those aged 75+. All ECGs with AF showed AF during the complete recording. Of participants with AF, 29.7% had experienced a fall vs. 19.6% of non-AF participants (p=0.007). Of participants with AF, 10.3% had experienced syncope, compared to 4.4% of non-AF participants (p=0.003).
Table 1 shows baseline characteristics. Fallers and those with syncope were older, reported more depressive symptoms, disability, cardiovascular conditions and diabetes than those without events. They had slower gait speed and used more psychotropic drugs. Participants with syncope were somewhat younger than participants with falls. In addition, participants with syncope were more often smokers, reported more lung disease, hypertension and use of cardiovascular medication.

Table 2 shows the occurrence of AF in study participants with and without falls or syncope. AF was more prevalent in participants with syncope compared to participants without syncope (5.4% vs 2.3%, p=0.003). AF was also more prevalent in fallers than non-fallers (3.6% vs 2.1%, p=0.006). Stratified for age-category, prevalence of AF was significantly higher in those with falls aged 65-74 years, and in those with syncope aged 50-64 years.
af falling: should one blame the heart?

TABLE 3. ASSOCIATION BETWEEN AF EN SYNCOPE (SELF-REPORTED FAINTS OR BLACKOUTS) OR FALLS IN THE PAST YEAR THROUGH MULTIVARIATE LOGISTIC REGRESSION ANALYSIS

<table>
<thead>
<tr>
<th>Bivariate OR (95%CI)</th>
<th>Model 1 OR (95%CI)</th>
<th>Model 2 OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any syncope‡</td>
<td>2.4 (1.3–4.5)**</td>
<td>2.3 (1.2–4.4)*</td>
</tr>
<tr>
<td>50-64y</td>
<td>4.7 (1.8–12.6)**</td>
<td>3.0 (1.9–13.9)**</td>
</tr>
<tr>
<td>65-74y</td>
<td>3.5 (0.8–3.0)</td>
<td>2.8 (0.8–3.3)</td>
</tr>
<tr>
<td>&gt;75y</td>
<td>3.0 (0.4–3.1)</td>
<td>3.6 (0.5–3.6)</td>
</tr>
<tr>
<td>Any fall‡</td>
<td>1.7 (1.1–2.7)**</td>
<td>3.5 (0.9–2.3)</td>
</tr>
<tr>
<td>50-64y</td>
<td>1.3 (0.6–3.1)</td>
<td>3.2 (0.8–2.3)</td>
</tr>
<tr>
<td>65-74y</td>
<td>1.8 (0.9–3.3)</td>
<td>2.0 (1.0–4.0)*</td>
</tr>
<tr>
<td>&gt;75y</td>
<td>1.2 (0.6–2.5)</td>
<td>1.5 (0.9–2.7)</td>
</tr>
</tbody>
</table>

Model 1: Adjusted for age, gender, and education. Model 2: Model 1 + gait speed, depressive symptoms, visual acuity, MMSE score, use of psychotropic drugs, use of cardiovascular drugs and medical history of stroke. Syncope: n=4693, falls: n=4696, 4.0% missing values. 95%CI: 95% confidence interval OR: Odds Ratio, Δ P<0.05, ** p<0.01, *** p<0.001

In a large cohort of community-dwellings aged 50 and older, objectively diagnosed AF was associated with syncope (self-reported faints or blackouts), independent of stroke, cardiovascular drugs and other confounders. AF was also associated with one or more falls in the past year in those aged 65-74 years.

To the best of our knowledge, this study is the first to report the association between AF and falls in the general population. However, AF has been associated with non-accidental falls in an ED-setting. Several studies on syncope in acute care settings have recognized arrhythmias as a cause of syncope, and a previous study has linked cardiac arrhythmia to syncope on a general population level. Within the same cohort, AF specifically was reported as a risk factor for recurrent syncope. The Framingham heart study reported no association between AF and syncope. Amnesia for loss of consciousness is common in syncope and fall events are often unobserved. Older persons may therefore report syncope as falls. Potentially, this explains why AF was associated with faints and blackouts in the younger age group (50-64 years), and with falls in the older age group (65-74 years). The proportion of participants aged 75+ was only 10% of the cohort, which may explain the lack of association between AF and falls in that group. Baseline characteristics in the present study also show that participants with syncope and falls share similar clinical characteristics, providing further evidence that these conditions indeed overlap.

Although the design of the current study limits us to demonstrate a causal relationship between AF, falls and syncope, several potential pathways can provide an underlying rationale for our findings. Paroxysmal AF is considered the most common type of AF to cause syncope, as the onset of AF can induce hemodynamic changes resulting in syncope. As AF was defined using 10-minute ECGs, we were unable to establish whether the AF detected was paroxysmal or persistent-type. Due to the brief time period of recordings however, it is likely that the majority of AF-cases represented subjects with a persistent-type AF. However, as paroxysmal AF in the course of time usually progresses into persistent forms of AF, potentially the mechanisms responsible for the association are similar. AF can lead to decreased cardiac output because of increased and/or irregular ventricular rate, and a reduction in the atrial contribution to ventricular filling. Furthermore, vagal stimulation has potential to elicit
(paroxysmal) AF, and the presence of atrial ectopy is associated with orthostatic hypotension. Orthostatic hypotension and vasovagal syncope are both important causes of falls and syncope on older persons, and this evidence highlights the potential role of AF in the causal chain between neurocardiovascular instability and syncope.

Cognitive impairment and depression, both important risk factors for falls, are associated with AF, potentially explained through the association between AF, cerebral hypoperfusion and white matter lesions. Furthermore, AF is associated with slower gait speed, which has been reported as a predictor for falls. However, adjustment for these potential confounders in our analysis did not weaken associations, thus strengthening the potential for an independent relationship between AF and syncope and falls. As AF is often concomitant with other cardiovascular conditions, potentially AF merely acts as a marker for these cardiovascular conditions. Adjustment for cardiovascular conditions resulted in loss of significance of the reported associations. However, ORs remained unchanged, indicating that loss of significance was likely due to lack of power.

The current study has some limitations. As the design of the study was cross-sectional, we cannot draw conclusions regarding potential causality, as further longitudinal studies are needed to explore this. Diagnosis of AF was based on ECGs obtained during the health assessment, whereas falls or blackouts may have occurred at any time in the preceding year. Therefore, we are unable to conclude that subjects had AF during their event. A number of paroxysmal AF cases were likely missed, potentially leading to an underestimation of the associations. Furthermore, ECG recording was only performed in participants who attended the health assessment. It is known that participants who did not attend the health assessment represent older and frailer group. As these participants are prone to both falls and AF, this might have led to an underestimation of the associations in the oldest age category. As recall of falls in the last year is less sensitive than collecting falls data prospectively, falls may be underreported in this sample. However, as the mean age of participants was 62 years and cognitive test scores were high, it is unlikely that poor recall of fall or syncope events accounted for the majority of this sample.

If future studies could demonstrate a causal relationship between AF and falls and syncope, this would have potential to contribute to practice-guidelines for falls and syncope. AF is the most common cardiac arrhythmia in older adults, and several treatment options exist. Some studies have shown an improvement of exercise capacity and ejection fraction in AF patients after cardioversion. Potentially, optimization of hemodynamic function in AF through adequate rate- or rhythm control could lead to a reduction in falls and syncope. This would require further study through randomized controlled trials. Furthermore, as over 30% of subjects with AF are unaware of their diagnosis, and those at high risk of stroke often receive inadequate treatment, detection of AF in community-dwellings could also add to the prevention of stroke and other AF-related events.

In summary, the results of our study show that AF was cross-sectionally associated with faints and blackouts in community-dwelling older adults aged 50+, and with falls in those aged 65-74 years. As AF may act as a risk-indicator for falls and syncope, early recognition of AF in older adults is warranted in subjects presenting with these events. However, further longitudinal studies are needed to explore a potential causal relationship between AF and falls and syncope.

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